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CLINICAL REVIEW

Preventing deep vein thrombosis in hospital inpatients

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BMJ 2007;335:147-51
doi:10.1136/bmj.39247.542477.AE

Most hospital inpatients are at risk of deep vein thrombosis (DVT) and the associated complications of fatal or non-fatal pulmonary embolism and post-thrombotic syndrome. Recognised risk factors for DVT are generally related to one or more elements of Virchow's triad (stasis, vessel injury, and hypercoagulability), and include surgery, trauma, immobilisation, malignancy, use of oestrogens, heart or respiratory failure, and smoking (box 1).[1] Surveillance studies have found that the absolute risk of DVT is 10%-20% among general medical patients and up to 40%-80% in patients having hip surgery, knee surgery, or major trauma (table).[1]

It is difficult to predict which at-risk patients will develop DVT, and fatal pulmonary embolism can occur without warning without prior clinical suspicion. It is therefore important to take appropriate preventive measures for all hospital inpatients and to determine which of them warrant additional prophylaxis. Major guidelines on DVT prophylaxis have been produced by the American College of Chest Physicians,[1] the Institute for Clinical Systems Improvement,[2] the Scottish Intercollegiate Guidelines Network,[3] the American College of Obstetricians and Gynecologists,[4] and the National Institute for Health and Clinical Excellence (NICE).[5]

What are the methods of DVT prophylaxis?

Methods of DVT prophylaxis include general measures: the use of aspirin, mechanical prevention with graduated compression stockings, and intermittent pneumatic compression devices. Anticoagulants often used include unfractionated heparin (UFH) (usually given as 5000 units two or three times daily), low molecular weight heparins (LMWH) (usually enoxaparin or dalteparin), vitamin K antagonists (most often warfarin, but also acenocoumarol, phenindione, and dicoumarol), and fondaparinux (a selective factor Xa inhibitor) (box 2).[6]

How well do the mechanical methods of prophylaxis work?

A Cochrane review found that graduated compression stockings were effective in reducing rates of DVT for general medical and surgical patients whether they were used alone or in addition to other DVT prophylaxis. In nine studies comparing graduated compression stockings with no prophylaxis, rates of DVT were reduced from 27% to 13%, and in seven studies the addition of the stockings to background prophylaxis further reduced DVT rates from 15% to 2%.[7]

Additionally, a recent randomised but non-blinded clinical trial found that the use of graduated compression stockings in patients with DVT reduced the risk of post-thrombotic syndrome from 49% to 26%.[8] A meta-analysis of 57 studies found that intermittent pneumatic compression devices for the thigh and calf were effective in reducing rates of DVT when compared with placebo (from 29% to 11%) and with graduated compression stockings alone (from 15% to 8%).[9] A recent systematic review found that graduated compression stockings, intermittent pneumatic compression devices, and foot pumps reduce the risk of DVT in surgical patients by two thirds when used as monotherapy and by an additional 50% when added to drug prophylaxis.[10] The review also found that mechanical prophylaxis in surgical patients may reduce the risk of pulmonary embolism by about two fifths.[10]

Mechanical prophylaxis must be used with caution, however, if a patient has peripheral arterial insufficiency.[1]

Can aspirin be used to reduce the risk of DVT?

Aspirin has been considered as a possible low risk measure for preventing DVT. One large trial has documented a reduction in symptomatic DVT and fatal pulmonary embolism with aspirin prophylaxis, with only a small increased risk of minor bleeding that did not require transfusion.[11] Although the guidelines from the American College of Chest Physicians

SOURCES AND SELECTION CRITERIA

I identified sources for this review by searching Medline (www.ncbi.nlm.nih.gov/entrez/query.fcgi), the Cochrane Collaboration (www.cochrane.org) and the National Guideline Clearinghouse (www.guideline.gov/) in November 2005 for references to prevention of deep vein thrombosis. I selected reviews, guidelines, and studies if they discussed prevention of deep vein thrombosis in medical or surgical inpatients

and the Institute for Clinical Systems Improvement recommend against relying on aspirin for prevention DVT because of the risk of increased bleeding,[1 2] the guidelines from the Scottish Intercollegiate Guidelines Network advocate aspirin as an effective prophylaxis in surgical patients because of its efficacy in reducing fatal pulmonary embolism.[3]

How can we reduce risk of DVT in general medical patients?

Medical patients account for up to a quarter of venous thromboembolic events in the general population.[1] UFH and LMWH have been studied for DVT prophylaxis in the general medical population, and a meta-analysis published in 2000 found that both heparin types reduced the rates of DVT and clinical pulmonary embolism by 56%-58%. No differences were found between the two types of heparin in the rates of DVT, clinical pulmonary embolism, or death, but use of LMWH carried a lower risk of major bleeding.[12] Guidelines from the American College of Chest Physicians, the Institute for Clinical Systems Improvement, and the Scottish Intercollegiate Guidelines Network support ambulation for all patients if possible, and recommend LMWH or UFH for medical patients with heart failure or respiratory disease or with substantial immobility plus additional risk factors for DVT. Mechanical prophylaxis may be considered in all immobile patients and should be used for those who cannot receive anticoagulants.[1-3]

How can we reduce risk of DVT in surgical patients?

A recent systematic review found that, across all types of surgery, monotherapy with oral anticoagulants halved the risk of DVT. However, oral anticoagulants also doubled the risk of major bleeding and were less effective than heparins at preventing DVT.[10]

Box 1 | Risk factors for deep vein thrombosis (adapted from Geerts et al[1])

Stasis
- Surgery, trauma, immobility, paresis
- Increasing age
- Pregnancy and postpartum
- Heart or respiratory failure
- Obesity

Vessel injury
- Previous deep vein thrombosis
- Smoking
- Varicose veins
- Central venous catheterisation

Hypercoagulability
- Increasing age
- Malignancy or cancer therapy
- Oestrogen therapy (contraception or hormone replacement)
- Acute medical illness
- Inflammatory bowel disease
- Nephrotic syndrome
- Myeloproliferative disorders
- Paroxysmal nocturnal haemoglobinuria
- Inherited or acquired thrombophilia

Absolute risk of deep vein thrombosis in hospital inpatients

Patient group	Prevalence of deep vein thrombosis (%)
General medical	10-20
General surgery	15-40
Major gynaecological surgery	15-40
Stroke	20-50
Hip or knee arthroplasty, hip fracture surgery	40-60
Major trauma	40-80
Critical care	10-80

General and other non-orthopaedic surgery

Patients admitted to hospital for general surgery are at moderate risk of DVT, and a 1997 meta-analysis of 33 studies showed that both UFH and LMWH were effective in reducing rates of DVT and pulmonary embolism in general surgery patients.[13] The meta-analysis found no difference in major bleeding between the two treatments, but LMWH showed a 25% relative risk reduction in the risk of minor bleeding.

A more recent meta-analysis based on published randomised controlled trials confirmed that LMWH reduced rates of asymptomatic and symptomatic DVT and rates of pulmonary embolism in general surgery patients compared with placebo[14]; it also found that high quality studies showed no difference between LMWH and UFH in terms of efficacy (reduction of DVT or pulmonary embolism) or safety (risk of bleeding). These findings were confirmed by a second meta-analysis published the same year, based on original patient data, which again found that both types of heparins were equally effective and equally safe for reducing DVT in general surgery patients.[15]

Guidelines from the American College of Chest Physicians, the Institute for Clinical Systems Improvement, and the Scottish Intercollegiate Guidelines Network recommend early mobilisation for general surgery patients at low risk of DVT; UFH or LMWH for patients with risk factors for DVT (including age), and the addition of mechanical prophylaxis to LMWH or UFH for those with multiple risk factors for DVT.[1-3] The NICE guidelines recommend that all surgical inpatients are offered graduated compression stockings (unless contraindicated) from the time they are admitted and that general surgery patients with one or more risk factors for DVT are also given LMWH or fondaparinux.[5]

Patients having major gynaecological surgery have a 7%-45% risk of DVT, and 1% of those with DVT may have a fatal pulmonary embolism. A Cochrane review of eight trials found evidence that, compared with placebo, 5000 units of subcutaneous UFH when started perioperatively and given two or three times daily for seven days reduced rates of DVT in women with malignancy, and, in one trial, warfarin given 6 mg daily reduced rates of DVT in women without malignancy.[16] The review found no difference in

DVT rates when UFH was compared with warfarin or with LMWH. None of the studies in the review were able to show a reduction in pulmonary embolism.

Minimal research has been conducted on mechanical methods of DVT prophylaxis for major gynaecological surgery. Guidelines from the American College of Obstetricians and Gynecologists recommend that patients at moderate or high risk of DVT (such as those having major surgery or who have malignancy or other risk factors) should receive prophylaxis with either thigh high graduated compression stockings placed intraoperatively and continued until the patient is ambulatory, or UFH or LMWH started preoperatively and continued until discharge.[4] The American College of Chest Physicians and the Scottish Intercollegiate Guidelines Network also recommend UFH or LMWH, with use of intermittent pneumatic compression devices or graduated compression stockings if anticoagulation is contraindicated.[1 3] NICE recommends mechanical prophylaxis for all patients, with the addition of LMWH for those with one or more risk factors for DVT.[5]

Box 2 | Methods of prophylaxis against DVT in hospital inpatients

- Graduated compression stockings
- Intermittent pneumatic compression
- Aspirin
- Unfractionated heparin
- Low molecular weight heparins (enoxaparin, dalteparin)
- Vitamin K antagonists (warfarin, acenocoumarol, phenindione, and dicoumarol)
- Fondaparinux

NICE guidelines and continuing controversies in thromboprophylaxis

Considerable controversy has followed publication of the NICE guideline on surgical thromboprophylaxis.[5] "Rapid responses" to a summary of the guidelines published in the *BMJ*[25] and to an accompanying editorial[26] identified several issues central to the controversy.

Disagreement continues between researchers and guideline authors about whether recommendations for DVT prophylaxis should be based on evidence that recommended measures reduce surrogate outcomes such as asymptomatic DVT or pulmonary embolism, or based solely on evidence of reduction in patient oriented outcomes such as morbidity or all cause mortality.

Concern has been expressed that the NICE guideline recommends mechanical DVT prophylaxis as the first line measure for non-orthopaedic surgery, whereas other guidelines[1-3] recommend starting with consideration of pharmacological prophylaxis. In fact, both NICE and the other major guidelines do recommend some form of pharmacological prophylaxis for patients with DVT risk factors. The difference is that NICE recommends mechanical prophylaxis for all surgical patients, whereas other major guidelines recommend early ambulation for patients at low risk of DVT. Disagreement remains, however, about whether age becomes a risk factor at age 40 or age 60.

Although the NICE guideline addresses DVT prophylaxis for surgical patients, calls for increased attention to thromboprophylaxis in medical patients are balanced by questions over the underlying data on morbidity and mortality from DVT in hospitalised medical patients.

Appropriate DVT prophylaxis for patients having spinal surgery, with the attendant risk of postoperative epidural haematoma, remains a subject of ongoing controversy.

Debate continues over the most effective methods of ensuring that practising doctors implement guideline based measures for DVT prophylaxis (such as electronic reminders and mandatory prophylaxis policies).

Application of guidelines to individual patients must integrate evidence based recommendations with a thorough understanding of the complexity of an individual patient's clinical situation.

Colorectal surgery may carry a higher risk of DVT than other general surgery procedures, and a Cochrane review in 2003 found that both LMWH and low dose UFH reduced risk of DVT and pulmonary embolism to the same extent, while the use of graduated compression stockings in addition to a heparin provided additional protection.[17] Patients having major open urological procedures often have multiple risk factors for DVT (including age and immobility). Little high quality evidence relates to this population, but guidelines favour using prophylaxis with UFH, LMWH, graduated compression stockings, or intermittent pneumatic compression devices in urology patients at high risk.[1 3 5] Patients having major vascular surgery (such as aortoiliac or aortofemoral surgery or aortic aneurysm resection) usually also have multiple risk factors for DVT, but as these procedures are usually accompanied by antiplatelet therapy, it is difficult to tell whether DVT prophylaxis confers an independent benefit. Guidelines recommend UFH or LMWH for DVT prevention if vascular surgery patients have additional thrombotic risk factors.[1 3 5]

Orthopaedic surgery

Patients having major orthopaedic surgery are at particularly high risk of DVT, and methods of prophylaxis have been extensively investigated. Two meta-analyses found that rates of DVT after total knee arthroplasty were much lower with intermittent pneumatic compression devices or LMWH (17%-29%) than with aspirin or warfarin (45%-53%).[18 19]

A Cochrane review of DVT prophylaxis after hip fracture surgery found that although both UFH and LMWH reduced lower limb DVT, the two heparins did not differ in efficacy; the review found no reduction in rates of pulmonary embolism with either of the heparins.[20] The review found insufficient data to evaluate the efficacy of intermittent pneumatic compression devices. A more recent meta-analysis of multiple vitamin K antagonists in orthopaedic surgery (including warfarin, acenocoumarol, phenindione, and dicoumarol) confirmed their effectiveness in reducing DVT

SUMMARY POINTS

Appropriate use of prophylaxis against deep vein thrombosis (DVT) in hospital inpatients is important for reducing the risk of fatal and non-fatal pulmonary embolism and post-thrombotic complications

For patients at low risk of DVT, ambulation is important, and mechanical methods of prophylaxis (such as graduated compression stockings and intermittent pneumatic compression devices) can provide added protection

Patients at higher risk of DVT should be considered for guideline based anticoagulation with low molecular weight heparin, unfractionated heparin, or vitamin K antagonists unless clearly contraindicated

Fondaparinux may provide additional prophylactic options

The place of aspirin in DVT prophylaxis remains controversial

To ensure adequate prophylaxis against DVT, doctors should be encouraged to follow appropriate guidelines

and clinical pulmonary embolism compared with placebo and in reducing DVT compared with intermittent pneumatic compression devices but still found they were less effective than LMWH for reducing DVT.[21] The same review found no difference between vitamin K antagonists and LMWH in the rates of wound haematoma. Meta-analyses have been unable to detect significant differences in DVT rates when comparing different currently recommended LMWH dosing regimens, or when comparing preoperative and postoperative initiation of LMWH prophylaxis.[22 23]

ADDITIONAL EDUCATIONAL RESOURCES

Resources for healthcare professionals

- Prevention of venous thromboembolism: the seventh ACCP conference on antithrombotic and thrombolytic therapy. www.chestjournal.org/cgi/content/full/126/3_suppl/338S
- Prophylaxis of venous thromboembolism. A national clinical guideline. Scottish Intercollegiate Guidelines Network. 2002. www.sign.ac.uk/pdf/sign62.pdf
- Venous thromboembolism prophylaxis. Institute for Clinical Systems Improvement. Institute for Clinical Systems Improvement. 2005. www.icsi.org
- Venous thromboembolism: reducing the risk of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in inpatients undergoing surgery. National Institute for Health and Clinical Excellence. 2007. http://guidance.nice.org.uk/CG46.
- Towards evidence-based guidelines for the prevention of venous thromboembolism: systematic reviews of mechanical methods, oral anticoagulation, dextran and regional anaesthesia as thromboprophylaxis. www.hta.ac.uk/execsumm/summ949.htm

Resources for patients

- Deep vein thrombosis: what you should know. http://familydoctor.org/online/famdocen/home/seniors/common-older/800.html
- Deep vein thrombosis (DVT). www.patient.co.uk/showdoc/23068982/
- CG46 Venous thromboembolism: Understanding NICE guidance. http://guidance.nice.org.uk/CG46/publicinfo/pdf

Current guidelines from the American College of Chest Physicians and the Institute for Clinical Systems Improvement recommend LMWH, vitamin K antagonists, or fondaparinux for elective hip or knee arthroplasty. These same methods, plus UFH are also recommended for hip fracture surgery, and either of the heparins should be started after hospital admission if fracture repair is going to be delayed. Prophylaxis should continue at least 10 days after major orthopaedic surgery and preferably up to four to five weeks after hip replacement or hip fracture surgery.[1 2] The Scottish Intercollegiate Guidelines Network places more emphasis on the use of aspirin for DVT prophylaxis in elective orthopaedic surgery and hip fracture surgery.[3] NICE recommends mechanical prophylaxis plus either LMWH or fondaparinux for elective orthopaedic surgery and hip fracture surgery, with continuation of the heparin or fondaparinux for four weeks after hip fracture surgery and hip replacement in patients with risk factors for DVT.[5]

Trauma patients

Major trauma can place patients at particularly high risk of DVT or pulmonary embolism. The American College of Chest Physicians and the Scottish Intercollegiate Guidelines Network recommend LMWH for prophylaxis, with mechanical prophylaxis if the risk of bleeding precludes using anticoagulants.[1 3]

Summary

Appropriate use of DVT prophylaxis in hospital inpatients is important for reducing the risk of post-thrombotic complications as well as fatal and non-fatal pulmonary embolism. One of the most important steps in ensuring adequate prophylaxis against DVT is encouraging doctors to follow appropriate guidelines. A meta-analysis of interventions to improve compliance with guidelines found that strategies using electronic or paper based audit and feedback, or some other active reminder, were much more successful at improving rates of prophylaxis compared with passive education or dissemination of guidelines.[24]

For patients at low risk of DVT, ambulation is important, and mechanical methods of prophylaxis can provide added protection. Patients at higher risk of DVT should be considered for guideline based anticoagulation with LMWH, UFH, or vitamin K antagonists unless clearly contraindicated. Fondaparinux is a newer agent that may provide additional prophylactic options. The place of aspirin in DVT prophylaxis remains controversial.

Contributors: WEC is the sole contributor.
Competing interests: None declared.
Provenance and peer review: Not commissioned; externally peer reviewed.

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Accepted: 13 June 2007

The magnetic resonance egg timer

Unless something is happening, an x ray department can seem as uninteresting as an empty garage or aircraft hangar, but it is unethical to let visitors watch patients being examined. Fortunately, when the distinguished members of the Cirencester Science and Technology Society visited us to learn about radiological scanning, one of our secretaries agreed to act as a model, so demonstrating ultrasonography was not a problem. The visitors could see her heart and aorta pulsating, learn how a Doppler signal can be used to assess vascular flow, and witness how abdominal anatomy can be obscured by calcium in the ribs or air in the bowel.

A selection of foods and other items hidden in a cardboard box proved a popular way to demonstrate computed tomography. The visitors enjoyed being quizzed about the contents of the box, and having to distinguish cherries from grapes, a banana from a courgette, and a bruised apple from a sound one. They were also asked to distinguish a length of skirting board from a piece of "tongue-and-groove" plank, and the grain of the timber was shown exquisitely. Scans were completed in seconds, sections in all three orthogonal planes were quickly constructed, and post-processing techniques such as surface rendering were demonstrated.

We showed off magnetic resonance imaging (MRI) using a different phantom, a chicken carcase filled with eggs. The MR images not only revealed the detail of the chicken's anatomy but also distinguished each egg's embryo, yolk, and albumen. The differences between a fresh egg, a bad egg, and a chocolate cream egg were discernable, and one egg was made invisible by wrapping it in aluminium foil. The foil acts like a Faraday cage: it is a barrier to the passage of the radio waves which cause the resonance of protons on which MR signal is dependent.

An unforeseen effect, however, was how cooking an egg changes its MR signal. The albumen of a fresh egg seems white on T2 images, but the signal is lost on cooking so the white turns to black. The change from white to black extends in from the outside as the egg cooks. When an egg is ready to eat and the albumen has solidified, the white of an egg is completely black on T2 images. This occurs, as may be guessed from breakfast experiences, after boiling for a little over three minutes.

Our finding suggested commercial potential, but there are practical constraints. The actual process of scanning takes a minute or two to complete, and the egg has to be cooked at a distance from the scanner to prevent the egg pan and heat source becoming stuck to the magnet. Moving a boiling egg in and out of the scanner is hardly practicable and, even if these matters could be solved, an MR egg timer is unlikely to become a cost effective alternative to the standard sandglass.

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